Remarks

Claims 17, 19, 22, 24-27 and 44 are canceled herein and new claims 45-56 are added herein. Applicants reserve the right to pursue the subject matter of the canceled claims in continuing applications. Support for new claim 45 can be found, *inter alia*, in Examples 9-11 of the specification. Support for new claims 46-47 can be found, *inter alia*, at paragraph 674 of the specification and Figures 37A-37C. Support for new claims 48-51 can be found, *inter alia*, at paragraphs 651-653 of the specification. Support for new claims 52-56 can be found, *inter alia*, in original claims 24-27. New claims 45-56 do not add new matter to the application. Claims 45-56 are pending in the application.

I. Rejection of the Claims Under 35 U.S.C. § 103(a)

Claims 17, 19, 22, 24-27 and 44 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Hartley *et al.* (*Genome Res., 10*:1788-1795, 2000) and Melchner and Hoffken (*Blut, 57*:1-5, 1988). (Office Action, page 3.) Applicants respectfully disagree but in order to expedite prosecution Applicants have canceled claims 17, 19, 22, 24-27 and 44 and added new claims 45-56.

The Examiner asserts that Hartley *et al.* discloses DNA cloning using site-specific recombination which may be used for protein expression and that Melchner and Hoffken describe recombinant retroviruses containing a foreign gene which may be used for gene transfer into hemopoietic cells. (Office Action, page 3.)

Vectors used in methods of the claimed invention include safety features intended to lessen the probability of a vector component becoming incorporated into a replication competent retrovirus. These Safety features include:

1) Lack of sufficient retroviral components to form a retroviral replication complex.
2) Use of multiple vectors which encode different components for forming retroviral particles.
3) Lack of sufficient homology to undergo homologous recombination with each other or the first and second nucleic acid molecules. This reduces the likelihood of

homologous recombination between the vectors or with retroviruses which may be resident in cells (see dependent claim 47).

4) Lack of long terminal repeats in vectors not intended for incorporation into retroviral particles.

New claim 45 is directed, in part, to a method of constructing a recombinant retrovirus wherein a first nucleic acid molecule lacks "retroviral sequences which produce retroviral gene products and which comprises a 5'-long terminal repeat, a 3'-long terminal repeat, a packaging signal" and "introducing the nucleic acid molecule generated in step (b), with at least three additional nucleic acid molecules which encode retroviral proteins, into a cell that packages the nucleic acid molecule generated in step (b)." Claim 46 further recites that elements necessary for proper packaging of a retrovirus are missing from the at least three additional nucleic acid molecules while claim 47 further recites that "the nucleic acid molecule of step (b), the at least three additional nucleic acid molecules lack sufficient homology to undergo homologous recombination with each other or the first and second nucleic acid molecules."

As noted above, these steps provide important advantages to the presently claimed method. In situations where the claimed methods may be used to insert genes into an organism, it is important that the possibility of unintended recombination events, with adventitious agents that may be present in the recipient organism, be reduced. In the claimed method, genes encoding components required for packaging are separated into multiple nucleic acid molecules which lack sufficient homology to undergo homologous recombination, helping to lessen the possibility of generating a replication-competent retrovirus. Further, because the nucleic acid molecules encoding the packaging proteins lack LTRs and a packaging sequence, the probability that these structural proteins are expressed in the transduced target cell is reduced and therefore the possibility of producing a replication-competent retrovirus is lessened.

Applicants assert that neither Hartley *et al.* or Melchner and Hoffken, alone or in combination, teach or suggest the presently claimed method. In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 103(a).

II. Double Patenting

Claims 17 and 44 stand rejected on the ground of non-statutory obviousness type double patenting as being unpatentable over claims 1, 17 and 18 of U.S. Patent No. 7,198,924. (Office Action, page 6.) Applicants again defer responding to this ground of rejection until patentable subject matter has been determined, at which time Applicants will consider filing a terminal disclaimer.

Conclusion

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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